

General

Guideline Title

Acute kidney injury. Prevention, detection and management of acute kidney injury up to the point of renal replacement therapy.

Bibliographic Source(s)

National Clinical Guideline Centre. Acute kidney injury. Prevention, detection and management of acute kidney injury up to the point of renal replacement therapy. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Aug. 39 p. (Clinical guideline; no. 169).

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

The wording used in the recommendations in this guideline (for example words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation) and is defined at the end of the "Major Recommendations" field.

Assessing Risk of Acute Kidney Injury (AKI)

Identifying AKI in Patients with Acute Illness

Investigate for AKI, by measuring serum creatinine and comparing with baseline, in adults with acute illness if any of the following are likely or present:

- Chronic kidney disease (adults with an estimated glomerular filtration rate [eGFR] less than 60 ml/min/1.73 m² are at particular risk)
- Heart failure
- Liver disease
- Diabetes
- History of AKI
- Oliguria (urine output less than 0.5 ml/kg/hour)
- Neurological or cognitive impairment or disability, which may mean limited access to fluids because of reliance on a carer
- Hypovolaemia
- Use of drugs with nephrotoxic potential (such as non-steroidal anti-inflammatory drugs [NSAIDs], aminoglycosides, angiotensin-converting

enzyme [ACE] inhibitors, angiotensin II receptor antagonists [ARBs], and diuretics) within the past week, especially if hypovolaemic

- Use of iodinated contrast agents within the past week
- Symptoms or history of urological obstruction, or conditions that may lead to obstruction
- Sepsis
- Deteriorating early warning scores
- Age 65 years or over

Investigate for AKI, by measuring serum creatinine and comparing with baseline, in children and young people with acute illness if any of the following are likely or present:

- Chronic kidney disease
- Heart failure
- Liver disease
- History of AKI
- Oliguria (urine output less than 0.5 ml/kg/hour)
- Young age, neurological or cognitive impairment, or disability, which may mean limited access to fluids because of reliance on a parent or carer
- Hypovolaemia
- Use of drugs with nephrotoxic potential (such as NSAIDs, aminoglycosides, ACE inhibitors, ARBs and diuretics) within the past week, especially if hypovolaemic
- Symptoms or history of urological obstruction, or conditions that may lead to obstruction
- Sepsis
- A deteriorating paediatric early warning score
- Severe diarrhoea (children and young people with bloody diarrhoea are at particular risk)
- Symptoms or signs of nephritis (such as oedema or haematuria)
- Haematological malignancy
- Hypotension

Identifying AKI in Patients with No Obvious Acute Illness

- Be aware that in adults, children and young people with chronic kidney disease and no obvious acute illness, a rise in serum creatinine may indicate AKI rather than a worsening of their chronic disease.
- Ensure that AKI is considered when an adult, child or young person presents with an illness with no clear acute component and has any of the following:
 - Chronic kidney disease, especially stage 3B, 4, or 5, or urological disease
 - New onset or significant worsening of urological symptoms
 - Symptoms suggesting complications of AKI
 - Symptoms or signs of a multi-system disease affecting the kidneys and other organ systems (for example, signs or symptoms of AKI, plus a purpuric rash)

Assessing Risk Factors in Adults Having Iodinated Contrast Agents

Before offering iodinated contrast agents to adults for non-emergency imaging, investigate for chronic kidney disease by measuring eGFR or by checking an eGFR result obtained within the past 3 months.

Before offering iodinated contrast agents to adults for emergency or non-emergency imaging, assess their risk of AKI. Be aware that increased risk is associated with:

- Chronic kidney disease (adults with an eGFR less than 40 ml/min/1.73 m² are at particular risk)
- Diabetes but only with chronic kidney disease (adults with an eGFR less than 40 ml/min/1.73 m² are at particular risk)
- Heart failure
- Renal transplant
- Age 75 years or over
- Hypovolaemia
- Increasing volume of contrast agent
- Intra-arterial administration of contrast agent

Ensure that risk assessment does not delay emergency imaging.

Include the risks of developing AKI in the routine discussion of risks and benefits of the imaging procedure. Follow the recommendations on shared decision-making in [Patient experience in adult NHS services](#) [] (NICE clinical guidance 138).

Assessing Risk Factors in Adults Having Surgery

Assess the risk of AKI in adults before surgery. Be aware that increased risk is associated with:

- Emergency surgery, especially when the patient has sepsis or hypovolaemia
 - Intraoperative surgery
 - Chronic kidney disease (adults with an eGFR less than 60 ml/min/1.73 m² are at particular risk)
 - Diabetes
 - Heart failure
 - Age 65 years or over
 - Liver disease
 - Use of drugs with nephrotoxic potential in the perioperative period (in particular, NSAIDs after surgery)
- Use the risk assessment to inform a clinical management plan.

Include the risks of developing AKI in the routine discussion of risks and benefits of surgery. Follow the recommendations on shared decision-making in [Patient experience in adult NHS services](#) [] (NICE clinical guidance 138).

Preventing AKI

Ongoing Assessment of the Condition of Patients in Hospital

Follow the recommendations in [Recognition of and response to acute illness in adults in hospital](#) [] (NICE clinical guideline 50) on the use of track and trigger systems (early warning scores) to identify adults who are at risk of AKI because their clinical condition is deteriorating or is at risk of deteriorating.

When adults are at risk of AKI, ensure that systems are in place to recognise and respond to oliguria (urine output less than 0.5 ml/kg/hour) if the track and trigger system (early warning score) does not monitor urine output.

Consider using a paediatric early warning score to identify children and young people admitted to hospital who are at risk of AKI because their clinical condition is deteriorating or is at risk of deteriorating.

- Record physiological observations at admission and then according to local protocols for given paediatric early warning scores.
- Increase the frequency of observations if abnormal physiology is detected.

If using a paediatric early warning score, use one with multiple-parameter or aggregate weighted scoring systems that allow a graded response and:

- Define the parameters to be measured and the frequency of observations.
- Include a clear and explicit statement of the parameters, cut-off points, or scores that should trigger a response.

If using a paediatric early warning score, use one with multiple-parameter or aggregate weighted scoring systems that measure:

- Heart rate
- Respiratory rate
- Systolic blood pressure
- Level of consciousness
- Oxygen saturation
- Temperature
- Capillary refill time

When children and young people are at risk of AKI because of risk factors listed under "Identifying AKI in Patients with Acute Illness" above:

- Measure urine output
- Record weight twice daily to determine fluid balance
- Measure urea, creatinine, and electrolytes
- Think about measuring lactate, blood glucose, and blood gases

Preventing AKI in Adults Having Iodinated Contrast Agents

Offer intravenous volume expansion to adults having iodinated contrast agents if:

- They are at increased risk of contrast-induced AKI because of risk factors listed under "Assessing Risk Factors in Adults Having Iodinated Contrast Agents," above or
 - They have an acute illness
- Offer either isotonic sodium bicarbonate or 0.9% sodium chloride.

Consider temporarily stopping ACE inhibitors and ARBs in adults having iodinated contrast agents if they have chronic kidney disease with an eGFR less than 40 ml/min/1.73 m².

Discuss care with a nephrology team before offering iodinated contrast agent to adults with contraindications to intravenous fluids if:

- They are at increased risk of contrast-induced AKI, or
- They have an acute illness, or
- They are on renal replacement therapy

Monitoring and Preventing Deterioration in Patients with or at High Risk of AKI

Consider electronic clinical decision support systems (CDSS) to support clinical decision-making and prescribing, but ensure they do not replace clinical judgement.

When acquiring any new CDSS or systems for electronic prescribing, ensure that any systems considered:

- Can interact with laboratory systems
- Can recommend drug dosing and frequency
- Can store and update data on patient history and characteristics, including age, weight, and renal replacement therapy
- Can include alerts that are mandatory for the healthcare professional to acknowledge and review

Seek advice from a pharmacist about optimising medicines and drug dosing in adults, children, and young people with or at risk of AKI.

Consider temporarily stopping ACE inhibitors and ARBs in adults, children, and young people with diarrhoea, vomiting or sepsis until their clinical condition has improved and stabilised.

Detecting AKI

Detect AKI, in line with the (p)RIFLE¹, AKIN² or KDIGO³ definitions, by using any of the following criteria:

- A rise in serum creatinine of 26 µmol/litre or greater within 48 hours
- A 50% or greater rise in serum creatinine known or presumed to have occurred within the past 7 days
- A fall in urine output to less than 0.5 ml/kg/hour for more than 6 hours in adults and more than 8 hours in children and young people
- A 25% or greater fall in eGFR in children and young people within the past 7 days

Monitor serum creatinine regularly⁴ in all adults, children, and young people with or at risk of AKI.

¹Risk, Injury, Failure, Loss, End stage renal disease, (p) refers to the paediatric classification.

²Acute Kidney Injury Network

³Kidney Disease: Improving Global Outcomes

⁴The GDG did not wish to define 'regularly' because this would vary according to clinical need but recognised that daily measurement was typical while in hospital.

Identifying the Cause(s) of AKI

Identify the cause(s) of AKI and record the details in the patient's notes.

Urinalysis

Perform urine dipstick testing for blood, protein, leucocytes, nitrites, and glucose in all patients as soon as AKI is suspected or detected. Document the results and ensure that appropriate action is taken when results are abnormal.

Think about a diagnosis of acute nephritis and referral to the nephrology team when an adult, child, or young person with no obvious cause of AKI has urine dipstick results showing haematuria and proteinuria, without urinary tract infection or trauma due to catheterisation.

Ultrasound

Do not routinely offer ultrasound of the urinary tract when the cause of the AKI has been identified.

When pyonephrosis (infected and obstructed kidney[s]) is suspected in adults, children and young people with AKI, offer immediate ultrasound of the urinary tract (to be performed within 6 hours of assessment).

When adults, children and young people have no identified cause of their AKI or are at risk of urinary tract obstruction, offer urgent ultrasound of the urinary tract (to be performed within 24 hours of assessment).

Managing AKI

Relieving Urological Obstruction

Refer all adults, children, and young people with upper tract urological obstruction to a urologist. Refer immediately when one or more of the following is present:

- Pyonephrosis
- An obstructed solitary kidney
- Bilateral upper urinary tract obstruction
- Complications of AKI caused by urological obstruction

When nephrostomy or stenting is used to treat upper tract urological obstruction in adults, children, and young people with AKI, undertake as soon as possible and within 12 hours of diagnosis.

Pharmacological Management

Do not routinely offer loop diuretics to treat AKI.

Consider loop diuretics for treating fluid overload or oedema while:

- An adult, child or young person is awaiting renal replacement therapy, or
- Renal function is recovering in an adult, child, or young person not receiving renal replacement therapy

Do not offer low-dose dopamine to treat AKI.

Referring for Renal Replacement Therapy

Discuss any potential indications for renal replacement therapy with a nephrologist, paediatric nephrologist, and/or critical care specialist immediately to ensure that the therapy is started as soon as needed.

When an adult, child, or young person has significant comorbidities, discuss with them and/or their parent or carer and within the multidisciplinary team whether renal replacement therapy would offer benefit. Follow the recommendations on shared decision-making in [Patient experience in adult NHS services](#) (NICE clinical guidance 138).

Refer adults, children, and young people immediately for renal replacement therapy if any of the following are not responding to medical management:

- Hyperkalaemia
- Metabolic acidosis
- Symptoms or complications of uraemia (for example, pericarditis or encephalopathy)
- Fluid overload
- Pulmonary oedema

Base the decision to start renal replacement therapy on the condition of the adult, child, or young person as a whole and not on an isolated urea, creatinine, or potassium value.

When there are indications for renal replacement therapy, the nephrologist and/or critical care specialist should discuss the treatment with the adult, child, or young person and/or their parent or carer as soon as possible and before starting treatment. Follow the recommendations on shared

decision-making in [Patient experience in adult NHS services](#) (NICE clinical guidance 138).

Referring to Nephrology

Refer adults, children and young people with AKI to a nephrologist, paediatric nephrologist, and/or critical care specialist immediately if they meet criteria for renal replacement therapy listed under "Referring for Renal Replacement Therapy," above.

Do not refer adults, children or young people to a nephrologist or paediatric nephrologist when there is a clear cause for AKI and the condition is responding promptly to medical management, unless they have a renal transplant.

Consider discussing management with a nephrologist or paediatric nephrologist when an adult, child, or young person with severe illness might benefit from treatment, but there is uncertainty as to whether they are nearing the end of their life.

Refer adults, children and young people in intensive care to a nephrology team when there is uncertainty about the cause of AKI or when specialist management of kidney injury might be needed.

Discuss the management of AKI with a nephrologist or paediatric nephrologist as soon as possible and within 24 hours of detection when one or more of the following is present:

- A possible diagnosis that may need specialist treatment (for example, vasculitis, glomerulonephritis, tubulointerstitial nephritis, or myeloma)
- AKI with no clear cause
- Inadequate response to treatment
- Complications associated with AKI
- Stage 3 AKI (according to [p]RIFLE, AKIN, or KDIGO criteria)
- A renal transplant
- Chronic kidney disease stage 4 or 5

Monitor⁵ serum creatinine after an episode of AKI. Consider referral to a nephrologist or paediatric nephrologist when eGFR is 30 ml/min/1.73 m² or less in adults, children, and young people who have recovered from an AKI.

Consider referral to a paediatric nephrologist for children and young people who have recovered from an episode of AKI but have hypertension, impaired renal function or 1+ or greater proteinuria on dipstick testing of an early morning urine sample.

⁵The frequency of monitoring should be based on the stability and degree of renal function at the time of discharge.

Information and Support for Patients and Carers

Discuss immediate treatment options, monitoring, prognosis, and support options as soon as possible with people with AKI and/or, if appropriate, their parent or carer. Follow the recommendations on patient views and preferences and shared decision-making in [Patient experience in adult NHS services](#) (NICE clinical guidance 138).

Give information about long-term treatment options, monitoring, self-management, and support to people who have had AKI (and/or their parent or carer, if appropriate) in collaboration with a multidisciplinary team appropriate to the person's individual needs.

Give information about future care to people needing renal replacement therapy after discharge following AKI. This should include information about the frequency and length of dialysis sessions and the preparation needed (such as having a fistula or peritoneal catheter).

Discuss the risk of developing AKI, particularly the risk associated with conditions leading to dehydration (for example, diarrhoea, and vomiting) and drugs with nephrotoxic potential (including over-the-counter NSAIDs), with people who are at risk of AKI, particularly those who have:

- Chronic kidney disease with an eGFR less than 60 ml/min/1.73 m²
 - Neurological or cognitive impairment or disability, which may mean limited access to fluids because of reliance on a carer
- Involve parents and carers in the discussion if appropriate

Definitions:

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some

interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer...') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Clinical Algorithm(s)

A National Institute for Health and Care Excellence (NICE) care pathway titled "Acute Kidney Injury Overview" is available from the [NICE Web site](#) .

Scope

Disease/Condition(s)

Acute kidney injury

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Emergency Medicine

Family Practice

Geriatrics

Internal Medicine

Nephrology

Pediatrics

Pharmacology

Preventive Medicine

Urology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Hospitals

Nurses

Patients

Physician Assistants

Physicians

Guideline Objective(s)

- To provide best practice advice on prevention, detection, and management of acute kidney injury up to the point of renal replacement therapy
- To emphasise early intervention and stress the importance of risk assessment and prevention, early recognition and treatment

Target Population

Adults, children (older than 1 month) and young people (up to 18 years)

Note: Particular consideration will be given to the needs of older patients (65 years and older) and people at high risk of developing acute kidney injury (AKI), such as people with chronic kidney disease and urological disorders. The guideline does not cover neonates (less than 1 month), pregnant women and AKI in renal transplant patients. It does not cover aspects of renal replacement therapy beyond the decision to initiate it such as type, modality and length.

Interventions and Practices Considered

1. Investigation for acute kidney injury (AKI) by measuring serum creatinine and comparing with baseline
2. Identification of AKI in patients with no obvious illness
3. Assessment of risk factors in adults having iodinated contrast agents
 - Measuring estimated glomerular filtration rate (eGFR)
 - Discussion of risks and benefits of the imaging procedure
4. Assessment of risk factors in adults having surgery
5. Ongoing assessment of condition of patients in hospital
 - Use of early warning scores
 - Monitoring for oliguria
6. Preventing AKI in adults having iodinated contrast agents
 - Intravenous volume expansion
 - Temporarily stopping angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists (ARBs)

- Discussion of care with a nephrology team
- 7. Monitoring and preventing deterioration in patients with or at high risk of AKI
 - Use of electronic clinical decision support systems (CDSS)
 - Consultation with pharmacist
 - Temporarily stopping ACE inhibitors and ARBs
- 8. Detecting AKI
 - Use of specific laboratory criteria
 - Monitor serum creatinine regularly in all adults, children and young people at risk
- 9. Identification of causes of AKI
 - Urinalysis
 - Ultrasound
- 10. Managing AKI
 - Relieving urological obstruction (nephrostomy, stenting)
 - Pharmacological management (loop diuretics, not recommended routinely)
 - Referral for renal replacement therapy
- 11. Information and support for patients and carers

Note: Low-dose dopamine was considered but not recommended.

Major Outcomes Considered

- Sensitivity, specificity, positive predictive value, negative predictive value and likelihood ratio of diagnostic tests
- Incidence of acute kidney injury
- Cardiovascular events
- All-cause mortality
- Number of patients needing renal replacement therapy
- Length of hospital stay
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE) (see the "Availability of Companion Documents" field for the full version of this guidance).

Developing the Review Questions and Outcomes

Review questions were developed in a PICO framework (patient, intervention, comparison, and outcome) for intervention reviews, and with a framework of population, index tests, reference standard, and target condition for reviews of diagnostic test accuracy. This was to guide the literature searching process and to facilitate the development of recommendations by the Guideline Development Group (GDG). They were drafted by the NCGC technical team and refined and validated by the GDG. The questions were based on the key clinical areas identified in the scope (see Appendix A in the full version of the original guideline document; see the "Availability of Companion Documents" field).

For each review, question, the GDG chose up to 7 outcomes identifying which outcomes were critical to their decision making and which were

important. This distinction helped the GDG to make judgements about the importance of the different outcomes and their impact on decision making. For example, mortality will usually be considered a critical outcome and would be given greater weight when considering the clinical effectiveness of an intervention than an important outcome with less serious consequences. The GDG decide on the relative importance in the review protocol before seeing the review.

Searching for Evidence

Clinical Literature Search

Systematic literature searches were undertaken to identify evidence within published literature in order to answer the review questions as per The Guidelines Manual 2009 (see the "Availability of Companion Documents" field). Clinical databases were searched using relevant medical subject headings, free-text terms, and study type filters where appropriate. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English language. All searches were conducted on core databases, MEDLINE, EMBASE, and The Cochrane Library. Additional subject specific databases were used for some questions: Cumulative Index to Nursing and Allied Health Literature (CINAHL) for risk assessment tools, paediatric early warning scores, computerised decision tools, urinalysis, ultrasound, referring to nephrology, and information and support for patients and carers; PsycINFO for information and support for patients and carers. All searches were updated on 3 January 2013. No papers after this date were considered.

Search strategies were checked by looking at reference lists of relevant key papers, checking search strategies in other systematic reviews, and asking the GDG for known studies. The questions, the study types applied, the databases searched, and the years covered can be found in Appendix D in the full version of the original guideline document.

During the scoping stage, a search was conducted for guidelines and reports on the websites listed below and on organisations relevant to the topic. Searching for grey literature or unpublished literature was not undertaken. All references sent by stakeholders were considered.

- Guidelines International Network database (www.g-i-n.net)
- National Guideline Clearinghouse (www.guideline.gov/)
- NICE (www.nice.org.uk)
- National Institutes of Health Consensus Development Program (consensus.nih.gov/)
- National Library for Health (www.library.nhs.uk/)

Health Economic Literature Search

Systematic literature searches were also undertaken to identify health economic evidence within published literature relevant to the review questions. The evidence was identified by conducting a broad search relating to acute kidney injury in the National Health Service economic evaluation database (NHS EED), the Health Economic Evaluations Database (HEED), and health technology assessment (HTA) databases with no date restrictions. Additionally, the search was run on MEDLINE and EMBASE, with a specific economic filter. This was supplemented by additional searches that looked for economic papers specifically relating to contrast induced-acute kidney injury and computerised decision tools on NHS EED, HEED, HTA, Medline, and EMBASE, as it became apparent that some papers in this area were not being identified through the first search. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English language.

The search strategies for health economics are included in Appendix D in the full version of the original guideline document. All searches were updated on 3 January 2013. No papers published after this date were considered.

Evidence of Effectiveness

The evidence was reviewed following the steps shown schematically in Figure 1 in the full version of the original guideline document:

- Potentially relevant studies were identified for each review question from the relevant search results by reviewing titles and abstracts. Full papers were then obtained.
- Full papers were reviewed against pre-specified inclusion/exclusion criteria to identify studies that addressed the review question in the appropriate population (review protocols are included in Appendix C in the full version of the original guideline document).

Inclusion/Exclusion

The inclusion/exclusion of studies was based on the review protocols (see Appendix C in the full version of the original guideline document). The GDG was consulted about any uncertainty regarding inclusion/exclusion of selected studies. The guideline population was defined to be adults, children and young people. For some review questions, the review population was confined to special groups such as people at risk of acute

kidney injury (AKI), people with AKI, or people with chronic kidney disease.

Randomised trials, non-randomised trials, and observational studies (including prognostic studies) were included in the evidence reviews as appropriate. Laboratory studies (in vivo or in vitro) were excluded.

Conference abstracts were not automatically excluded from the review but were initially assessed against the inclusion criteria and reviewed only if no other full publication was available for a particular review question or if it provided further data on published studies. Literature reviews, letters and editorials, foreign language publications, and unpublished studies were excluded.

The review protocols are presented in Appendix C of the full version of the original guideline document. A full list of excluded studies with reasons for exclusion is available in Appendix I of the full version of the original guideline document.

Type of Studies

For most intervention reviews in this guideline, parallel randomised trials (RCTs) were included because they are considered the most robust type of study design that could produce an unbiased estimate of the intervention effects. For the prognostic review on the risk factors for acute kidney injury in children and young people, cross-sectional, prospective, and retrospective studies were included and for the prognostic review on predicting the outcome of acute kidney injury, prospective and retrospective cohort studies were included. Case control studies were not included.

Evidence of Cost-effectiveness

Literature Review

The health economist:

- Identified potentially relevant studies for each review question from the economic search results by reviewing titles and abstracts – full papers were then obtained.
- Reviewed full papers against pre-specified inclusion/exclusion criteria to identify relevant studies

Inclusion/Exclusion

Full economic evaluations (studies comparing costs and health consequences of alternative courses of action: cost–utility, cost–effectiveness, cost–benefit, and cost–consequence analyses) and comparative costing studies that addressed the review question in the relevant population were considered potentially includable as economic evidence.

Studies that only reported cost per hospital (not per patient), or only reported average cost effectiveness without disaggregated costs and effects, were excluded. Abstracts, posters, reviews, letters/editorials, foreign language publications, and unpublished studies were excluded. Studies judged to have an applicability rating of 'not applicable' were excluded (this included studies that took the perspective of a non–Organisation for Economic Co-operation and Development [OECD] country).

Remaining studies were prioritised for inclusion based on their relative applicability to the development of this guideline and the study limitations. For example, if a high quality, directly applicable UK analysis was available other less relevant studies may not have been included. Where exclusions occurred on this basis, this is noted in the relevant section.

For more details about the assessment of applicability and methodological quality see the economic evaluation checklist (the Guidelines Manual, and the health economics research protocol in Appendix C in the full version of the original guideline document).

Number of Source Documents

The number of studies identified for each clinical question is provided in Appendix E in the full version of the original guideline document (see the "Availability of Companion Documents" field).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Evidence of Effectiveness

The evidence was reviewed following the steps shown schematically in Figure 1 in the full version of the original guideline document:

- Relevant studies were critically appraised using the appropriate checklists as specified in The Guidelines Manual. For prognostic studies, quality was assessed using the checklist for Prognostic studies (NICE Guidelines Manual, 2009 [see the "Availability of Companion Documents" field]).
- Key information was extracted on the study's methods and PICO (patient, intervention, comparison, and outcome) factors and results were presented in evidence tables (see Appendix G in the full version of the original guideline document).
- Summaries of the evidence were generated by outcome (included in the relevant chapter writeups) and were presented in Guideline Development Group (GDG) meetings:
 - Randomised studies: meta-analysed, where appropriate, and reported in Grading of Recommendations Assessment, Development and Evaluation (GRADE) profiles.
 - Prognostic studies: assessing risk factors data were presented as a range of values, usually in terms of the relative effect as reported by the authors and where possible reported in the GRADE profile format.
 - Prognostic studies evaluating risk tools were presented as measures of prognostic test accuracy (sensitivity, specificity, positive, and negative predictive value). Coupled values of sensitivity and specificity were summarised in receiver operating characteristic (ROC) curves to allow visual comparison between different index tests (plotting data at different thresholds) and to investigate heterogeneity more effectively (given data were reported at the same thresholds). A meta-analysis could not be conducted because the studies reported data at various thresholds.

Twenty per cent (20%) of each of the above stages of the reviewing process was quality assured by the second reviewer to eliminate any potential of reviewer bias or error.

Methods of Combining Clinical Studies

Data Synthesis for Intervention Reviews

Where possible, meta-analyses were conducted to combine the results of studies for each review question using Cochrane Review Manager (RevMan5) software. Where studies reported data which could not be analysed by meta-analysis a narrative summary is provided.

Fixed-effects (Mantel-Haenszel) techniques were used to calculate pooled risk ratios (relative risk) for binary outcomes. For continuous outcomes,

measures of central tendency (mean), and variation (standard deviation) were required for meta-analysis. Data for continuous outcomes were analysed using an inverse variance method for pooling mean differences, and where the studies had different scales, standardised mean differences were used. A generic inverse variance option in Review Manager was used if any studies reported solely the summary statistics and 95% confidence interval (CI) (or standard error) – this included any hazard ratios reported. However, in cases where standard deviations were not reported per intervention group, the standard error for the mean difference was calculated from other reported statistics - p-values or 95% CIs; meta-analysis was then undertaken for the mean difference and standard error using the generic inverse variance method in Cochrane Review Manager (RevMan5) software.

Statistical heterogeneity was assessed by visually examining the forest plots, and by considering the chi-squared test for significance at $p < 0.1$ and the I-squared inconsistency statistic (with an I-squared value of more than 50% indicating considerable heterogeneity). Where considerable heterogeneity was present, sensitivity analyses were carried out. Sensitivity analyses were carried out looking at the subgroups which were pre-specified by the GDG. If the heterogeneity still remained, a random effects (DerSimonian and Laird) model was employed to provide a more conservative estimate of the effect.

For interpretation of the binary outcome results, differences in the absolute event rate were calculated using the GRADEpro software, for the median event rate across the control arms of the individual studies in the meta-analysis. The hazard ratio can be translated into an absolute difference in the proportion of patients who are event-free at a particular time point, assuming proportional hazards. This is calculated using GRADEpro software. Absolute risk differences were presented in the GRADE profiles and in clinical summary of findings tables, for discussion with the GDG.

Data Synthesis for Prognostic Factor Reviews

Odds ratio, relative risks, or hazard ratios, with their 95% CIs, from multivariate analyses were extracted from the papers, and standard errors were calculated from the 95% CIs. The log of the effect size with its standard error was entered into the generic inverse variance technique in the Cochrane Review Manager (RevMan5) software. For the Acute Kidney Injury Network (AKIN); Risk, Injury, Failure, Loss, and End-stage Kidney (RIFLE); and Kidney Disease: Improving Global Outcomes (KDIGO) review ratio of odds ratios were also calculated (see Sections 7.1.2 and 7.1.3 in the full version of the original guideline document for more information).

Coupled forest plots of sensitivity and specificity with their 95% CIs across studies (at various thresholds) were produced for each risk tool, using Cochrane Review Manager (RevMan5) software. In order to do that, 2×2 tables (the number of true positives, false positives, true negatives, and false negatives) were either directly taken from the study if given or derived from raw data, or were calculated from the set of test accuracy statistics.

To allow comparison between tests, summary ROC curves were generated for each prognostic test from the pairs of sensitivity and specificity calculated from the 2×2 tables, selecting one threshold per study. A ROC plot shows true positive rate (i.e., sensitivity) as a function of false positive rate (i.e., $1 - \text{specificity}$). Data were entered into Review Manager 5 software and ROC curves were fitted using the Moses Littenburg approach.

Area under the ROC curve (AUC) data for each study was also plotted on a graph, for each prognostic test: the AUC describes the overall prognostic accuracy across the full range of thresholds. The GDG agreed on the following criteria for AUC: 0.50-0.60 no discrimination; poor discrimination 0.60-0.70; fair discrimination 0.70-0.80; good discrimination 0.80-0.90 and excellent discrimination > 0.90 .

Heterogeneity or inconsistency amongst studies was visually inspected in the forest plots, if appropriate (only when there were similar thresholds). A prognostic meta-analysis was not conducted mainly because of the different thresholds across studies and the complexity of the analysis and time and resource constraints of this guideline development.

Data Synthesis for Diagnostic Test Accuracy Review

For diagnostic test accuracy studies, the following outcomes were reported: sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio. In cases where the outcomes were not reported, 2×2 tables were constructed from raw data to allow calculation of these accuracy measures. Summary ROC curves were generated where appropriate. The latter plot is normally used when diagnostic test accuracy studies explore the effect of different cut-off thresholds on sensitivity and specificity. A summary ROC curve is obtained by fitting a regression curve to pairs of sensitivity and specificity. The summary ROC curve and the area under it present a global summary of test performance and show the trade off between sensitivity and specificity. A symmetric, shoulder like ROC curve suggests that variability in the thresholds used could, in part, explain variability in study results. Weighted analyses are provided (by sample size). A good test is considered to be one in which the summary ROC curve is close to the 100% sensitivity, 100% specificity point. Heterogeneity is represented on a ROC curve by vertical displacements around the ROC curve, and this was examined in subgroup analyses.

Type of Analysis

Estimates of effect from individual studies were based on the author reported data. As a preference available case analysis (ACA) was used and if this was not reported intention to treat (ITT) analysis was then used. The ACA method is preferred to an ITT with imputation analysis, in order to avoid making assumptions about the participants for whom outcome data was not available, and furthermore assuming that those with missing outcome data have the same event rate as those who continue. In addition, ITT analysis tends to bias the results towards no difference, and therefore the effect may be smaller than in reality.

Appraising the Quality of Evidence by Outcomes

The evidence for outcomes from the included RCT and observational studies were evaluated and presented using an adaptation of the 'GRADE toolbox' developed by the international GRADE working group (<http://www.gradeworkinggroup.org/>). The software (GRADEpro) developed by the GRADE working group was used to assess the quality of each outcome, taking into account individual study quality and the meta-analysis results. The summary of findings was presented as two separate tables in this guideline. The 'Clinical/Economic evidence profile' table includes details of the quality assessment while the 'Clinical/Economic evidence summary of findings' table includes pooled outcome data, where appropriate, an absolute measure of intervention effect, and the summary of quality of evidence for that outcome. In this table, the columns for intervention and control indicate the sum of the sample size for continuous outcomes. For binary outcomes such as number of patients with an adverse event, the event rates (n/N: number of patients with events divided by sum of number of patients) are shown with percentages. Reporting or publication bias was only taken into consideration in the quality assessment and included in the Clinical evidence profile table if it was apparent.

The evidence for each outcome was examined separately for the quality elements listed and defined in Table 1 in the full version of the original guideline document and each graded using the quality levels listed in Table 2 in the full version of the original guideline document. The main criteria considered in the rating of these elements are discussed below. Footnotes were used to describe reasons for grading a quality element as having serious or very serious problems. The ratings for each component were summed to obtain an overall assessment for each outcome (see the "Rating Scheme for the Strength of the Evidence" field).

The GRADE toolbox is currently designed only for randomised trials and observational studies but the quality assessment elements and outcome presentation were adapted for prognostic and diagnostic accuracy studies.

Grading the Quality of Clinical Evidence

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using GRADE:

1. A quality rating was assigned, based on the study design. RCTs start HIGH and observational studies as LOW, uncontrolled case series as LOW or VERY LOW.
2. The rating was then downgraded for the specified criteria: Study limitations, inconsistency, indirectness, imprecision, and reporting bias. Observational studies were upgraded if there was: a large magnitude of effect, dose-response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have 'serious' or 'very serious' risk of bias was rated down -1 or -2 points respectively.
3. The downgraded/upgraded marks were then summed and the overall quality rating was revised. For example, all RCTs started as HIGH and the overall quality became MODERATE, LOW, or VERY LOW if 1, 2, or 3 points were deducted respectively.
4. The reasons or criteria used for downgrading were specified in the footnotes.

The details of criteria used for each of the main quality element are discussed further in Sections 3.3.7 to 3.3.10 in the full version of the original guideline document.

Evidence of Cost-effectiveness

Literature Review

The health economist:

- Critically appraised relevant studies using the economic evaluations checklist as specified in The Guidelines Manual.
- In this guideline no study was found that met the inclusion criteria and no summary of evidence was generated.

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

This guidance was developed in accordance with the methods outlined in the NICE Guidelines Manual 2009 (see the "Availability of Companion Documents" field).

A multidisciplinary Guideline Development Group (GDG) comprising professional group members and consumer representatives of the main stakeholders developed this guideline. The group met every 6-8 weeks during the development of the guideline.

Developing Recommendations

Over the course of the guideline development process, the GDG was presented with:

- Evidence tables of the clinical and economic evidence reviewed from the literature. All evidence tables are in appendix G of the full version of the original guideline document (see the "Availability of Companion Documents" field).
- Summary of clinical and economic evidence and quality (as presented in Chapters 5-10 in the full version of the original guideline document)
- Forest plots and summary receiver operating characteristic (ROC) curves (see Appendix H in the full version of the original guideline document)
- A description of the methods and results of the cost-effectiveness analysis undertaken for the guideline (see Appendix K in the full version of the original guideline document).

Recommendations were drafted on the basis of the GDG interpretation of the available evidence, taking into account the balance of benefits, harms, and costs. When clinical and economic evidence was of poor quality, conflicting or absent, the GDG drafted recommendations based on their expert opinion. The considerations for making consensus based recommendations include the balance between potential harms and benefits, economic or implications compared to the benefits, current practices, recommendations made in other relevant guidelines, patient preferences, and equality issues. The consensus recommendations were made through informal discussions in the GDG based on the best available evidence and GDG expertise. The GDG may also consider whether the uncertainty is sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation.

The main considerations specific to each recommendation are outlined in the Evidence to Recommendation Section preceding the recommendation section.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer...') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Cost Analysis

Undertaking New Health Economic Analysis

As well as reviewing the published economic literature for each review question, as described above, new economic analysis was undertaken by the health economist in selected areas. Priority areas for new health economic analysis were agreed by the Guideline Development Group (GDG) after formation of the review questions and consideration of the available health economic evidence.

The GDG identified Contrast Induced Acute Kidney Injury as the highest priority area for original economic modelling. Please see Chapter 6.2 of the full version of the original guideline document (see the "Availability of Companion Documents" field) for a full discussion of the rationale behind this decision.

The following general principles were adhered to in developing the cost-effectiveness analysis:

- Methods were consistent with the NICE reference case.
- The GDG was involved in the design of the model, selection of inputs, and interpretation of the results.
- Model inputs were based on the systematic review of the clinical literature supplemented with other published data sources where possible.
- When published data was not available GDG expert opinion was used to populate the model.
- Model inputs and assumptions were reported fully and transparently.
- The results were subject to sensitivity analysis and limitations were discussed.
- The model was peer-reviewed by another health economist at the National Clinical Guidelines Centre.

Full methods for the cost-effectiveness analysis for contrast induced acute kidney injury question are described in Appendix K of the original guideline document (see the "Availability of Companion Documents" field).

Cost-effectiveness Criteria

In general, an intervention was considered to be cost-effective if either of the following criteria applied (given that the estimate was considered plausible):

- a. The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
- b. The intervention cost less than £20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy.

If the GDG recommended an intervention that was estimated to cost more than £20,000 per QALY gained, or did not recommend one that was estimated to cost less than £20,000 per QALY gained, the reasons for this decision are discussed explicitly in the 'from evidence to recommendations' section of the relevant chapter with reference to issues regarding the plausibility of the estimate or to the factors set out in the National Institute for Health and Care Excellence (NICE) report 'Social value judgements: principles for the development of NICE guidance'.

If a study reported the cost per life year gained but not QALYs, the cost per QALY gained was estimated by multiplying by an appropriate utility estimate to aid interpretation. The estimated cost per QALY gained is reported in the economic evidence profile with a footnote detailing the life-years gained and the utility value used. When QALYs or life years gained are not used in the analysis, results are difficult to interpret unless one strategy dominates the others with respect to every relevant health outcome and cost.

See the individual chapters in the full version of the original guideline document (see the "Availability of Companion Documents" field) for discussions of the cost-effectiveness of specific recommendations.

In the Absence of Economic Evidence

When no relevant published studies were found, and a new analysis was not prioritised, the GDG made a qualitative judgement about cost effectiveness by considering expected differences in resource use between options and relevant UK National Health Service unit costs alongside the results of the clinical review of effectiveness evidence. The UK National Health Service costs reported in the guideline were those presented to

the GDG and they were correct at the time recommendations were drafted; they may have been revised subsequently by the time of publication. However, the GDG has no reason to believe they have been changed substantially.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guidance is subject to a six week public consultation and feedback as part of the quality assurance and peer review the document. All comments received from registered stakeholders are responded to in turn and posted on the National Institute for Health and Care Excellence (NICE) Web site when the pre-publication check of the full guideline occurs.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate prevention, detection, and management of acute kidney injury up to the point of renal replacement therapy

See the "Trade off between clinical benefits and harms" sections in the full version of the original guideline document for additional details about benefits of specific interventions.

Potential Harms

Assessing Risk of Acute Kidney Injury (AKI)

- Although there is minimal physical harm if patients with a falsely elevated risk of AKI undergo more intensive and more frequent monitoring, it is certainly not desirable from the patient's perspective in the presence of an already established illness or indeed from the perspective of the effective use of National Health Service (NHS) resources. If a false negative risk assessment results in a change to an inferior therapy, patients may come to harm in both the short and longer term.
- Risk assessment tools might potentially influence clinical decision making in a deleterious way. For example they may deter clinicians from deploying investigations and treatments which they consider potentially nephrotoxic but may otherwise benefit the patient. As such, risk assessment tools and the clinical behaviours they drive, need to be carefully considered.
- Another potential harm of the completion of risk-assessment tools is the impact on workload and time which may divert from other aspects of care although this is considered minimal in light of the potential benefit that can be derived if properly applied.

Preventing AKI

- The regular physiological assessment of children can cause anxiety to the child and their parents/carers, especially as such assessments are disruptive and cause disturbed sleep.
- There appeared to be a greater need for renal replacement therapy in the group given intravenous sodium bicarbonate versus no intravenous

hydration for prevention of contrast induced AKI. However the uncertainty of these effects were too large to make clear conclusions about clinical harm.

Detecting AKI

- It would be most important not to miss or delay diagnosis with a false negative result as this could lead to deterioration of the patient's clinical condition and increased complications (such as need for renal replacement therapy).
- False positive diagnosis could lead to unnecessary monitoring, blood tests, or other investigations, such as ultrasound scan, inappropriate administration of drugs, or withholding of drugs which would be given if the patient did not have AKI. This could lead to anxiety to patients and their families, and incorrect use of resources, with a likely increase in hospital stay. In a few cases, the false positive diagnosis might lead to unnecessary exposure to more invasive tests, exposure to radiation (e.g., if a computed tomography [CT] scan were performed).
- The Guideline Development Group (GDG) is aware that an acute creatinine increase of $\geq 26 \mu\text{mol/L}$ in people with a raised baseline creatinine (i.e., those with chronic kidney disease) may lead to a false positive diagnosis as noted by the Acute Kidney Injury Network (AKIN). This is because increments at the lower end of the spectrum may not exceed any expected change attributable to the combined pre-analytical, biological, and analytical variability between measurements. However, clinicians need to recognise the serious risks that AKI poses for a patient with chronic kidney disease. Until further evidence is available, the current definitions may serve to heighten awareness and increase vigilance.

Identifying the Cause of AKI

- The main potential harms with urine dipstick testing would arise in the case of false negative or false positive results. The implications of false negative results (under investigation of a potential glomerulonephritis as a cause of AKI) are minimised when a full evaluation and confirmation of urinalysis results using the correct procedure, as per the instructions of the dipstick manufacturer is undertaken. False positive haematuria on dipstick testing can lead to significant over investigation. In a patient with AKI, glomerular disease must be considered, which might require a series of relatively expensive biochemical and immunological tests (such as immunoglobulin, complement, autoimmune screen, antineutrophil cytoplasmic antibody [ANCA], anti-GBM). If doubt remains then renal biopsy might be required. This would represent a major additional cost, inconvenience and risk to the patient if it were undertaken on the basis of a false positive dipstick test.
- The clinical consequences of a failure to diagnose obstruction with ultrasound are potentially large. This must be balanced against the resource implications of routine ultrasound for all AKI, which is present in about 15% of hospital admissions.
- The potential risk of guidance which restricts access to ultrasound is that patients have undiagnosed obstruction with its attendant risks of worsening of AKI, severe sepsis (with an infected and obstructed urinary tract), development of AKI complications, exposure to the risks of renal replacement therapy, and potentially irreversible renal damage.
- It is acknowledged that ultrasound is not without 'harm' when unnecessarily undertaken in an unwell patient by adding further inconvenience and anxiety. Targeted ultrasound should mitigate against this potential harm.

Managing AKI

- Possible harms of early relief of upper tract urological obstruction by nephrostomy or stenting include complications of the procedure including bleeding, infection/sepsis and injury to the obstructed kidney leading to worsening of chronic kidney disease or end stage renal disease, or injury to nearby organs.
- Evidence from the review suggests that loop diuretics resulted in possibly more deaths and an increased requirement for renal replacement therapy compared to placebo or usual care. There was also a suggestion that loop diuretics could cause hearing loss, although it is uncertain whether this difference is clinically important because the event rate was low and hearing loss was not consistently reported.

Referring for Renal Replacement Therapy

- Early initiation of renal replacement therapy may result in patients who may have otherwise recovered renal function with conservative management alone to be exposed to the side effects of renal replacement therapy, in particular complications related to line insertion, risk of line infection, and bleeding complications as a result of anticoagulation.
- Renal replacement therapy in children is only available in paediatric intensive care units and in 11 paediatric nephrology centres in England and Wales, consequently often necessitating transfer over considerable distance with implications for the family and carers. Short term renal replacement therapy is offered at some adult centres for larger children and may be beneficial to stabilise critically ill children locally before transfer to a specialist centre to avoid unnecessary harm.
- Unlike in adults, the placement of dialysis access catheters in children almost always requires a general anaesthetic. The placement of these catheters is usually undertaken by consultant surgeons or anaesthetists whereas many adult access lines are placed by doctors in training. The early initiation of renal replacement therapy in children therefore requires careful consideration in light of the significant disruption for the

child and family and the health care resource required for this to be successful.

- Delayed initiation of renal replacement therapy may cause harm to both adults and children by increasing the risk of uraemic emergencies and by making fluid and electrolyte management more challenging. This may worsen patient outcomes.
- Of particular concern to the GDG was the issue regarding the initiation of renal replacement therapy in patients who had significant comorbidities in whom the decision to commence renal replacement therapy may be inappropriate and adversely affect quality of life. For example, individuals with significant comorbidities may be more appropriately managed by an end of life care pathway/conservative management strategy as renal replacement therapy would be intrusive and potentially cause psychological harm to the patient or the patient's carers or family. The above trade-offs apply to both adults and children.

Information and Support for Patients and Carers

As with any potentially serious medical condition, there will be some patients who might react negatively to the provision of information about their condition. It might cause anxiety or depression, even if the details are presented in a sensitive manner.

See the "Trade-off between clinical benefits and harms" sections of the full version of the original guideline document for additional details about harms of specific interventions.

Contraindications

Contraindications

For patients in whom intravenous fluids may be contraindicated, for example those with heart failure or chronic kidney disease with fluid overload, and at high risk of contrast-induced acute kidney injury, the Guideline Development Group recommended (by consensus) that their care should be discussed with a member of the nephrology team.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Care Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If the patient is under 16, their family or carers should also be given information and support to help the child or young person to make decisions about their treatment. Healthcare professionals should follow the [Department of Health's advice on consent](#) [redacted]. If someone does not have capacity to make decisions, healthcare professionals should follow the [code of practice that accompanies the Mental Capacity Act](#) [redacted] and the supplementary code of practice on deprivation of liberty safeguards. In Wales, healthcare professionals should follow [advice on consent from the Welsh Government](#) [redacted].
- The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.
- NICE has produced guidance on the components of good patient experience in adult National Health Service services. All healthcare professionals should follow the recommendations in [Patient experience in adult NHS services](#) [redacted] (NICE clinical guideline 138).
- If a young person is moving between paediatric and adult services, care should be planned and managed according to the best practice

guidance described in the Department of Health's Transition: getting it right for young people.

- Adult and paediatric healthcare teams should work jointly to provide assessment and services to young people with or at risk of acute kidney injury. Diagnosis and management should be reviewed throughout the transition process, and there should be clarity about who is the lead clinician to ensure continuity of care.
- For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision.

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Health and Care Excellence (NICE) has developed tools to help organisations implement this guidance. These are available on the [NICE Web site](#) (see also the "Availability of Companion Documents" field).

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

Identifying Acute Kidney Injury (AKI) in Patients with Acute Illness

- Investigate for AKI, by measuring serum creatinine and comparing with baseline, in adults with acute illness if any of the following are likely or present:
 - Chronic kidney disease (adults with an estimated glomerular filtration rate [eGFR] less than 60 ml/min/1.73 m² are at particular risk)
 - Heart failure
 - Liver disease
 - Diabetes
 - History of AKI
 - Oliguria (urine output less than 0.5 ml/kg/hour)
 - Neurological or cognitive impairment or disability, which may mean limited access to fluids because of reliance on a carer
 - Hypovolaemia
 - Use of drugs with nephrotoxic potential (such as non-steroidal anti-inflammatory drugs [NSAIDs], aminoglycosides, angiotensin-converting enzyme [ACE] inhibitors, angiotensin II receptor antagonists [ARBs], and diuretics) within the past week, especially if hypovolaemic
 - Use of iodinated contrast agents within the past week
 - Symptoms or history of urological obstruction, or conditions that may lead to obstruction
 - Sepsis
 - Deteriorating early warning scores
 - Age 65 years or over
- Investigate for AKI, by measuring serum creatinine and comparing with baseline, in children and young people with acute illness if any of the following are likely or present:
 - Chronic kidney disease
 - Heart failure
 - Liver disease
 - History of AKI
 - Oliguria (urine output less than 0.5 ml/kg/hour)
 - Young age, neurological or cognitive impairment or disability, which may mean limited access to fluids because of reliance on a parent or carer
 - Hypovolaemia
 - Use of drugs with nephrotoxic potential (such as NSAIDs, aminoglycosides, ACE inhibitors, ARBs, and diuretics) within the past week, especially if hypovolaemic
 - Symptoms or history of urological obstruction, or conditions that may lead to obstruction
 - Sepsis
 - A deteriorating paediatric early warning score
 - Severe diarrhoea (children and young people with bloody diarrhoea are at particular risk)

- Symptoms or signs of nephritis (such as oedema or haematuria)
- Haematological malignancy
- Hypotension

Assessing Risk Factors in Adults Having Iodinated Contrast Agents

- Before offering iodinated contrast agents to adults for emergency or non-emergency imaging, assess their risk of AKI. Be aware that increased risk is associated with:
 - Chronic kidney disease (adults with an eGFR less than 40 ml/min/1.73 m² are at particular risk)
 - Diabetes but only with chronic kidney disease (adults with an eGFR less than 40 ml/min/1.73 m² are at particular risk)
 - Heart failure
 - Renal transplant
 - Age 75 years or over
 - Hypovolaemia
 - Increasing volume of contrast agent
 - Intra-arterial administration of contrast agent
- Ensure that risk assessment does not delay emergency imaging.

Assessing Risk Factors in Adults Having Surgery

- Assess the risk of AKI in adults before surgery. Be aware that increased risk is associated with:
 - Emergency surgery, especially when the patient has sepsis or hypovolaemia
 - Intraperitoneal surgery
 - Chronic kidney disease (adults with an eGFR less than 60 ml/min/1.73 m² are at particular risk)
 - Diabetes
 - Heart failure
 - Age 65 years or over
 - Liver disease
 - Use of drugs with nephrotoxic potential in the perioperative period (in particular, NSAIDs after surgery).
- Use the risk assessment to inform a clinical management plan.

Ongoing Assessment of the Condition of Patients in Hospital

- When adults are at risk of AKI, ensure that systems are in place to recognise and respond to oliguria (urine output less than 0.5 ml/kg/hour) if the track and trigger system (early warning score) does not monitor urine output.

Detecting AKI

- Monitor serum creatinine regularly¹ in all adults, children, and young people with or at risk of AKI.

¹The GDG did not wish to define 'regularly' because this would vary according to clinical need but recognised that daily measurement was typical while in hospital.

Identifying the Cause(s) of AKI

- Identify the cause(s) of AKI and record the details in the patient's notes.

Ultrasound

- When adults, children, and young people have no identified cause of their AKI or are at risk of urinary tract obstruction, offer urgent ultrasound of the urinary tract (to be performed within 24 hours of assessment).

Referring to Nephrology

- Discuss the management of AKI with a nephrologist or paediatric nephrologist as soon as possible and within 24 hours of detection when one or more of the following is present:
 - A possible diagnosis that may need specialist treatment (for example, vasculitis, glomerulonephritis, tubulointerstitial nephritis, or myeloma)
 - AKI with no clear cause
 - Inadequate response to treatment

- Complications associated with AKI
- Stage 3 AKI (according to [p]RIFLE², AKIN³, or KDIGO⁴ criteria)
- A renal transplant
- Chronic kidney disease stage 4 or 5

²Risk, Injury, Failure, Loss, End stage renal disease, (p) refers to the paediatric classification.

³Acute Kidney Injury Network

⁴Kidney Disease: Improving Global Outcomes

Information and Support for Patients and Carers

- Give information about long-term treatment options, monitoring, self-management, and support to people who have had AKI (and/or their parent or carer, if appropriate) in collaboration with a multidisciplinary team appropriate to the person's individual needs.

Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

Foreign Language Translations

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Clinical Guideline Centre. Acute kidney injury. Prevention, detection and management of acute kidney injury up to the point of renal replacement therapy. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Aug. 39 p. (Clinical guideline; no. 169).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Aug

Guideline Developer(s)

National Guideline Centre - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Guideline Development Group (GDG)

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Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Development Group (GDG) members declared interests including consultancies, fee-paid work, share-holdings, fellowships, and support from the healthcare industry. At all subsequent GDG meetings, members declared arising conflicts of interest.

Members were either required to withdraw completely or for part of the discussion if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Appendix B in the full version of the original guideline document (see the "Availability of Companion Documents" field).

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) . Also available for download as a Kindle or EPUB ebook from the [NICE Web site](#) .

Availability of Companion Documents

The following are available:

- Acute kidney injury. Prevention, detection and management up to the point of renal replacement therapy. Full guideline. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Aug. 283 p. (Clinical guideline; no 169). Electronic copies: Available in Portable Document Format (PDF) from the [NICE Web site](#) .
- Acute kidney injury. Prevention, detection and management up to the point of renal replacement therapy. Appendices. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Aug. 445 p. (Clinical guideline; no 169). Electronic copies: Available in PDF from the [NICE Web site](#) .
- Acute kidney injury. Prevention, detection and management up to the point of renal replacement therapy. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Aug. (Clinical guideline; no 169). Electronic copies: Available from the [NICE Web site](#) .
- Acute kidney injury. Prevention, detection and management up to the point of renal replacement therapy. Clinical audit tools. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Aug. (Clinical guideline; no 169). Electronic copies: Available from the [NICE Web site](#) .
- Acute kidney injury. Prevention, detection and management up to the point of renal replacement therapy. Costing statement. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Aug. 7 p. (Clinical guideline; no 169). Electronic copies: Available in PDF from the [NICE Web site](#) .
- Acute kidney injury overview. NICE pathway. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Aug. Electronic copies: Available from the [NICE Web site](#) .
- The guidelines manual 2009. London (UK): National Institute for Health and Care Excellence (NICE); 2009 Jan. Electronic copies: Available in PDF from the [NICE Archive Web site](#) .

Patient Resources

The following is available:

- Acute kidney injury. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Aug. Electronic copies: Available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) . Also available for download as a Kindle or EPUB ebook from the [NICE Web site](#) . Also available in Welsh from the [NICE Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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